Suprachoroidal Delivery of RGX-314 for Diabetic Retinopathy Without CI-DME: Early Results from the Phase II ALTITUDE™ Study

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ASRS

Disclosures

- Consultant: REGENXBIO, Genentech/Roche

- Research Grants: Allergan, Aiviva, Amgen, Boehringer Ingelheim, Alcon, Aerpio, Kalvista, Ionis, Xplore, Mylan, Samsung, Novartis, Opthea, Chenghdu, Clearside, Astellas, Allegro, Alimera, Ophthotech/Iveric, Outlook, Gemini, Genentech, ThromboGenics, Tyrogenex, Graybug, Topcon, Optos, Gyroscope, Stealth Spiam, Aerie, Apellis, Roche, Novartis, OHR, Xplore, REGENXBIO, Kodiak , Zeiss, Annexon, and Regeneron Pharmaceuticals

RGX–314 for the Treatment of Diabetic Retinopathy (DR)

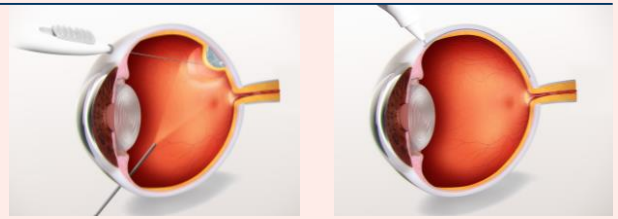
RGX–314 PRODUCT CANDIDATE

Vector: AAV8 | **Gene:** anti-VEGF fab

Route of administration:

Subretinal (nAMD) or

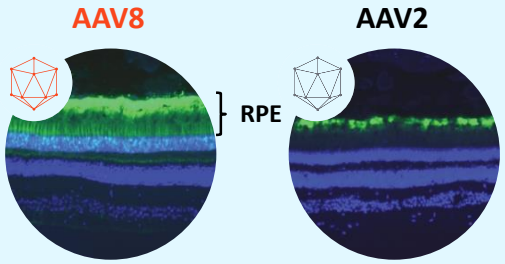
Suprachoroidal (nAMD/DR)



Mechanism of action:

Reducing leaky blood vessel formation by giving ocular cells the ability to produce an anti-VEGF fab

Improved AAV vector technology



More efficient gene delivery to the RPE[1]

+

Leveraging current standard of care in transgene

- FDA-approved mAbs and mAb fragments that inhibit VEGF are used for the prevention of DR complications
- **RGX–314 gene encodes an anti-VEGF mAb fragment (fab)**

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RGX–314: AAV8 encoding anti–VEGF fab

Potential for long-term therapeutic anti-VEGF expression

1. Vandenberghe et al. 2011 Science Translational Medicine

AAV: Adeno-Associated Virus.

ALTITUDE™: RGX-314 Phase II Clinical Trial in Diabetic Retinopathy

Primary Objective

- Evaluate proportion of patients with ≥2 step improvement in severity on the Diabetic Retinopathy Severity Scale (DRSS) at one year

Secondary Objectives

- Safety and tolerability of RGX-314
- Development of DR-related ocular complications
- Need for additional standard of care interventions

Subjects: Up to 60 total

- 18 study sites across the United States

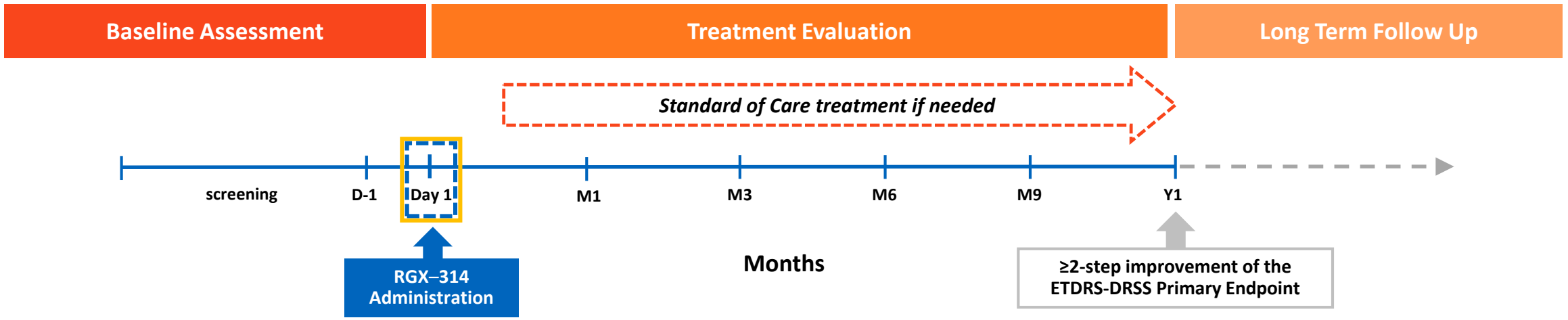
Route of Administration

- In-office SCS Microinjector™ delivers RGX-314 to the **suprachoroidal space**

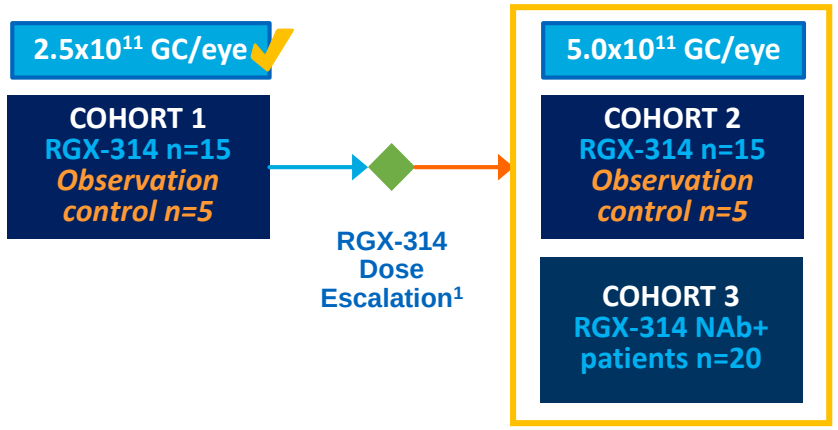
Key Inclusion Criteria

- Male or female ≥ 25 to 89 years of age with DR secondary to diabetes mellitus Type 1 or Type 2
- **Moderately Severe NPDR, Severe NPDR, or Mild PDR (DRSS levels 47-61)**
- No active CI-DME, CST < 320 µm
- Vision of 20/40 or better (≥ 69 Early Treatment Diabetic Retinopathy Study [ETDRS] letters) in the study eye
- No anti-VEGF injection(s) in prior 6 months

RGX-314 ALTITUDE™ Study Design



No prophylactic steroids given throughout the study



✓ Fully Enrolled

◆ IDMC Safety Review

1. Dose escalation safety review to occur two weeks after final subject in each cohort has been dosed.
NAb+ = AAV8 neutralizing antibody positive. Y1= 48 weeks.

ALTITUDE Baseline Characteristics (Cohort 1)

	Variable	Observational Control (N=5)	RGX-314 (N=15)	Total (N=20)
BASELINE[1]	**Mean Age** (Years)	51.0	50.7	50.8
	Gender – Female	1 (20%)	9 (60%)	10 (50%)
	Hemoglobin A1c	6.4	8.2	7.8
	Baseline DRSS score			
	47 (Moderately Severe, NPDR)	5 (100%)	5 (33.3%)	10 (50.0%)
	53 (Severe, NPDR)		2 (13.3%)	2 (10.0%)
	61 (Mild, PDR)		7 (46.7%)	7 (35%)
	65[2] (Moderate, PDR)		1 (6.7%)	1 (5%)
	Screening BCVA (Snellen equivalents)	87.6 (20/20)	78.1 (20/32)	80.5 (20/25)
	Screening OCT CRT (µm)	259.2	259.5	259.5
	Lens Status – Phakic n (%)	4 (80%)	13 (86.7%)	17 (85%)
PRIOR THERAPY	**Study Eye with anti-VEGF Injections in the Past 36-months** n (%)	0	5 (33.3%)	5 (25%)
	Months Since DR Diagnosis[3] – Mean	31.9	27.8	28.8

1. Ocular variables refer to study eye only.
2. After randomization, central reading center DRSS was scored as Grade 65 on final masked adjudication.
3. Based on randomization date.

ALTITUDE Safety Summary: Cohort 1

- RGX–314 was **well-tolerated** (n=15)
  - **1 SAE** that was **not considered drug-related**:
    - Vitreous hemorrhage in an untreated *fellow eye*
- **Common ocular TEAEs[1] in the study eye were not considered drug-related and were predominantly mild**:
  - Conjunctival hyperemia (2/15, 13%)
  - Conjunctival hemorrhage (2/15, 13%)
- One case of mild episcleritis[2] that resolved with topical corticosteroids
- **No intraocular inflammation** observed on slit-lamp examination

Data cut Sep 29, 2021

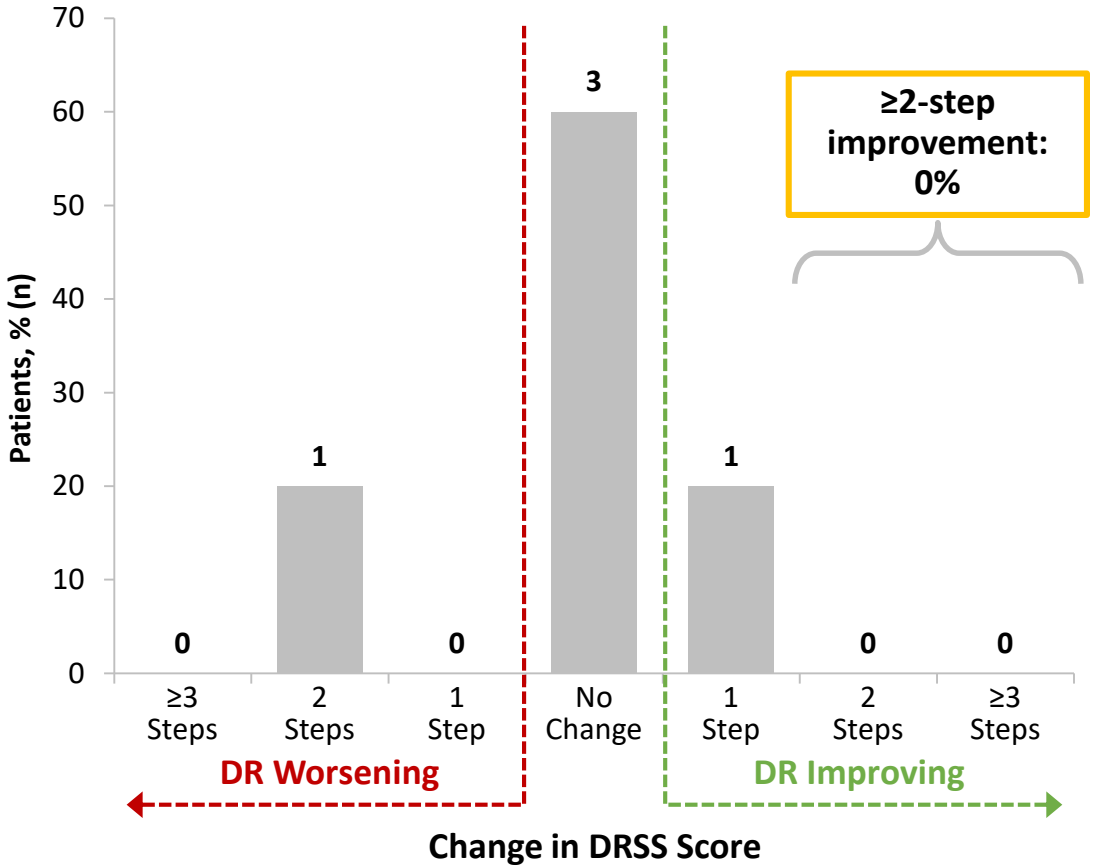
1. Common ocular TEAEs defined as ≥ 10% of RGX-314 treated study eyes.
2. Onset was 2-weeks post-dosing.

SAE: Serious Adverse Event; TEAE: Treatment Emergent Adverse Event.

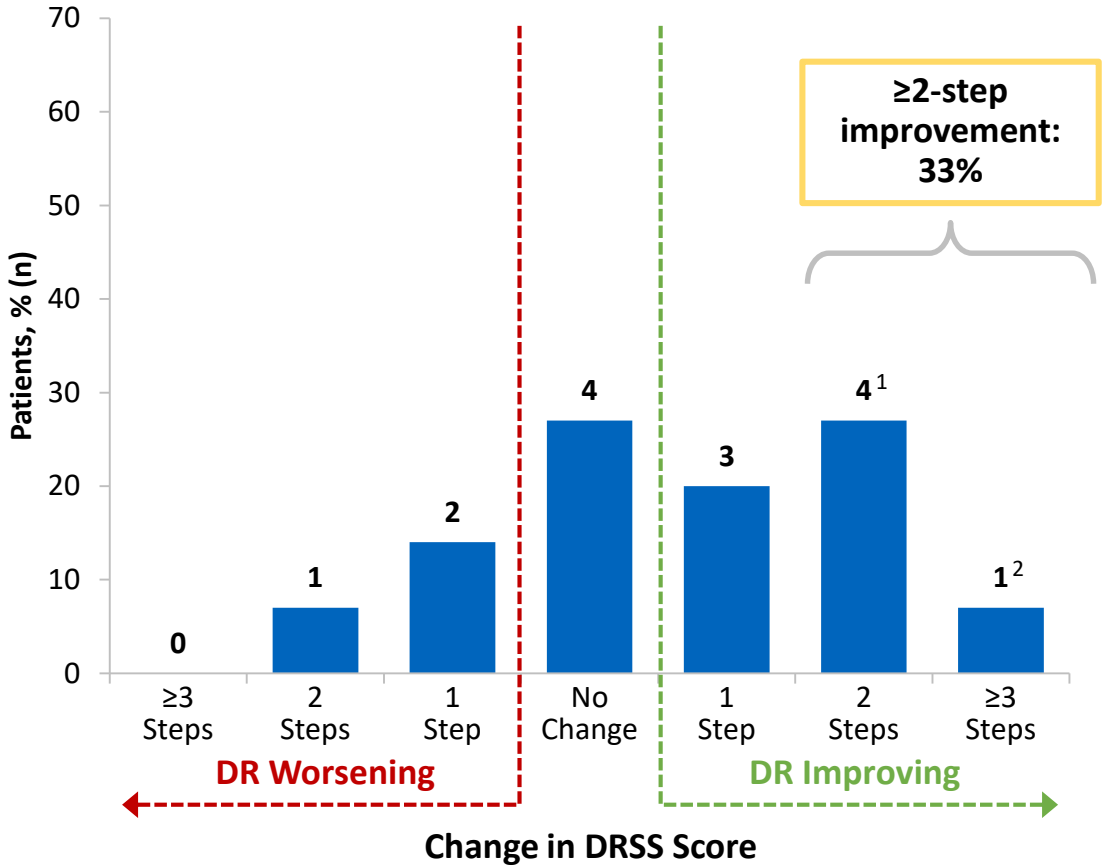
Cohort 1: Change in DRSS at Month 3

33% of RGX-314 Treated Patients Achieved a ≥2-Step Improvement

Observational Control (n=5)



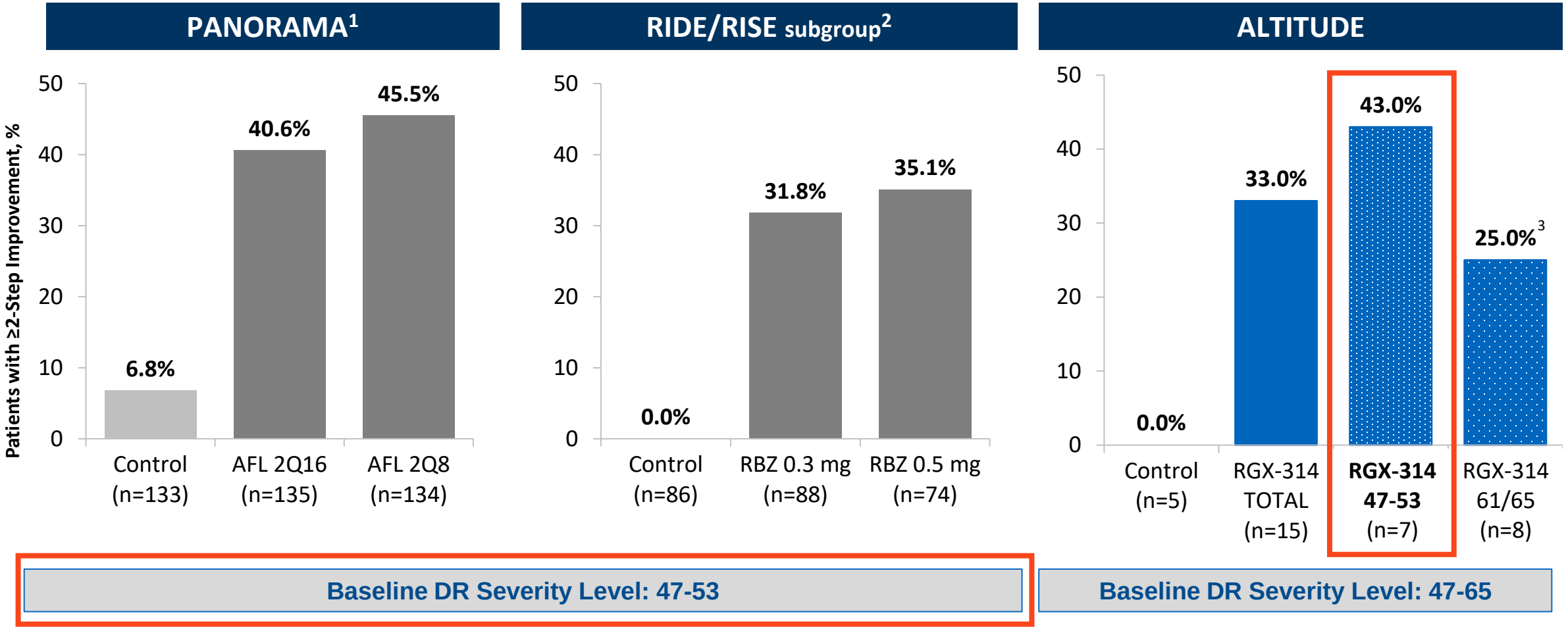
RGX-314 (n=15)



Data cut Sep 29, 2021

1. One study eye (DRSS 61 at baseline) received a single Lucentis injection 8 days after RGX-314 dosing for trace vitreous hemorrhage, which was 10 weeks prior to their 3 month visit when DRSS was assessed.
2. One patient had a 4-step improvement.

How do ALTITUDE Cohort 1 DRSS Outcomes at 3 Months Compare to Prior Clinical Trials?

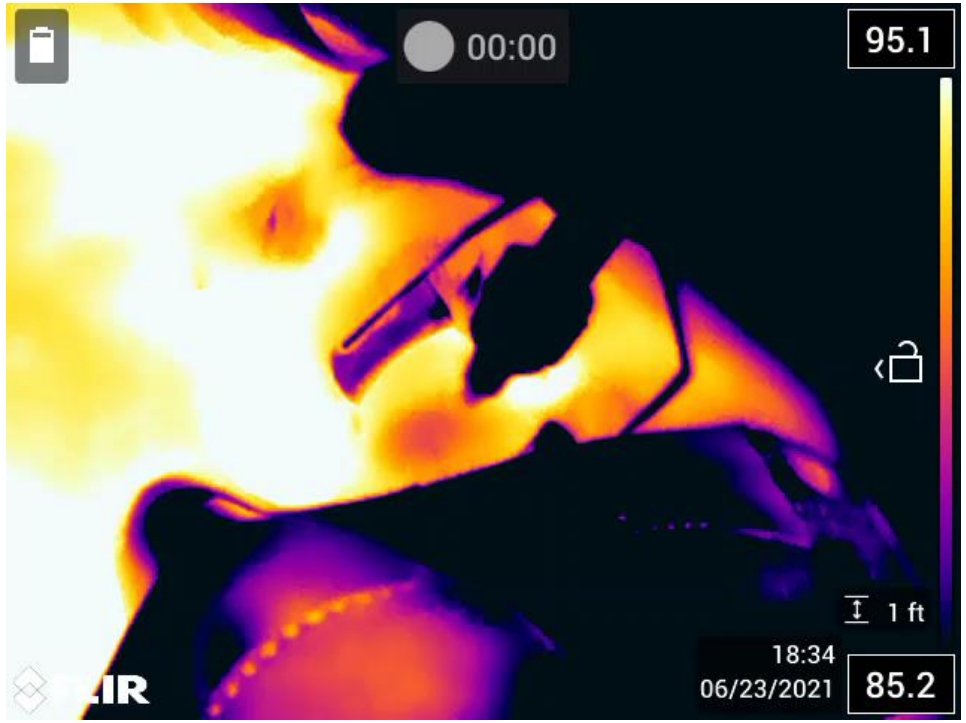


Data cut Sep 29, 2021

1. DRSS assessment at the 12 week timepoint was after 3 Q4W aflibercept (AFL) injections; EYLEA® (aflibercept) Injection full U.S. Prescribing Information. Regeneron Pharmaceuticals, Inc. March 2021.
2. DRSS assessment at the 3 month timepoint was after 3 Q4W ranibizumab (RBZ) injections; Wykoff CC et al. Ophthalmology Retina. 2018 DOI: (10.1016/j.oret.2018.06.005).
3. One patient had a 4-step improvement. Another study eye (DRSS 61 at baseline) received a single Lucentis injection 8 days after RGX-314 dosing for trace vitreous hemorrhage, which was 10 weeks prior to their 3 month visit when DRSS was assessed.

Summary of Initial Results from the Phase II ALTITUDE™ DR Study

- Suprachoroidal RGX-314 has been **well-tolerated** in Cohort 1 ($2.5x10^{11}$ GC/eye; n=15)
- **No intraocular inflammation**
  - No prophylactic corticosteroids administered
- In RGX-314 treated eyes, **33% achieved a ≥2 step improvement** in DRSS at 3 months



Video: D. Marcus

ALTITUDE study is currently enrolling Cohorts 2 and 3
(Dose level 2: $5.0x10^{11}$ GC/eye; NAb- and NAb+ patients)

Data cut September 29, 2021